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EXAMINER	
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ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,712	WAKAMIYA, NOBUTAKA	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 157,161-163,166-168,171-173,176-178,181-183,186-188,191-193,196,197,199-202,204-207,209-212 and 214-219.

Continuation of Disposition of Claims: Claims rejected are 157,161-163,166-168,171-173,176-178,181-183,186-188,191-193,196,197,199-202,204-207,209-212 and 214-219.

DETAILED ACTION

This Office Action is a reply to the Paper filed 21 December 2005 in response to the Non-Final Office Action mailed 21 July 2005. Claims 156-219 were considered in the 21 July Office Action. Claims 158-160, 164, 165, 169, 170, 174, 175, 179, 180 184, 185, 189, 190, 194, 195, 198, 203, 208 and 213 were canceled and claims 157, 161-163, 166-168, 171-173, 176-178, 181-183, 186-188, 191-193, 196, 197, 199-202, 204-207, 209-212 and 214-219 were amended in the 21 December Paper. Claims 157, 161-163, 166-168, 171-173, 176-178, 181-183, 186-188, 191-193, 196, 197, 199-202, 204-207, 209-212 and 214-219 are pending and under consideration.

Response to Amendment and Arguments

Rejection of claims 158-160, 164, 165, 169, 170, 174, 175, 179, 180 184, 185, 189, 190, 194, 195, 198, 203, 208 and 213 is rendered moot by the cancellation thereof.

Claim Rejections - 35 USC § 101

Claims 157, 161-163, 166-168, 171-173, 176-178, 181-183, 186-188, 191-193, 196, 197, 199-202, 204-207, 209-212 and 214-219 **stand rejected** under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The rejection was originally set forth in the Office Action 29 April 2003 and is summarized as follows:

On page 47 the specification sets forth the industrial applicability of the claimed invention as, "useful for investigating mechanisms of biological defense systems, and may

provide medical, experimental tools in which biological activities of the novel collectin are utilized. For example, vectors that can express the novel collectin, host cells comprising the vector with feasibility of expression, antibodies for the novel collectin, as well as probes for screening the related molecular species of the novel collectin can be provided. In addition, transgenic non-human animals...are provided, which may be utilized as disease model animals for studies on functions, or regulation of expression of the novel collectin". The specification provides no teachings regarding the unique function of the novel collectin (i.e., those functions arising from its novel structure) and only vague statements regarding its role in host defense. As the specification provides no specific function for the protein and does not identify a single specific condition that could be diagnosed or treated according to the teachings of the specification, it fails to provide a specific utility for the claimed polypeptide, nucleic acid and transgenic animal.

Furthermore, the asserted industrial applicability of the claimed Inventions is mostly directed to identifying the biological activity of the novel collectin and then utilizing the claimed products to diagnose or treat diseases based on that biological activity, whatever it might be. This amounts to an invitation to the skilled artisan to experiment in order to discover the utility of the claimed invention. Therefore the utility provided in the specification is not substantial.

With regard to well-established utility, the specification generally teaches that the novel collectin might be involved in innate immunity based on homology to a family of proteins having Ca^{2+}-dependent carbohydrate recognition regions and collagen-like regions known as collectins. The disclosure teaches only a fragment of the naturally occurring polypeptide, which does not comprise the membrane-spanning domain, and asserts that the disclosed polypeptide is

functionally related to a family of soluble proteins. Although it is possible that the extracellular fragment of the naturally occurring novel collectin might have activity similar to a known collectin, the skilled artisan would not be able to identify a well-established utility for the soluble portion of the novel collectin described in the application. Of the known collectins, the sequence set forth as SEQ ID NO:2 is most homologous to SP-D, a collectin found in pulmonary surfactant capable of binding microorganisms and stimulating chemotaxis of phagocytes and production of oxygen radicals (see Hansen *et al.* (1998) *Immunobiol.* 199:165-189, especially the second full paragraph on page 166). However, SEQ ID NO:2 shares only 35% identity with SP-D over 304 amino acids. The Office Action cites several teachings demonstrating that the art generally acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases such that a specific and substantial utility is readily apparent. The Office Action asserts, given that the structural homology of the instant SEQ ID NO: 2 to known collectins is 35%, at best, the function of the extracellular portion of the novel collectin described in the specification would be expected to be related to the function of other collectin family members in broad, general terms which do not suffice to assign a well-established utility to the claimed polypeptide.

Response to Arguments

In response to the *prima facie* case and arguments of record, Applicant again contends that the claimed invention has a well-established utility by virtue of its identification as a collectin. In particular, Applicant points to the teachings at page 2, lines 17-19 and Examples 1-3 of the specification, which, Applicant asserts, teaches that the novel collectin has homology with

known collectins. Applicant further cites a teaching at page 47, which purportedly teaches that the claimed invention has utilities of the same sorts as known lectins (final paragraph on page 8 of the remarks).

Further, Applicant notes that the USPTO has an entire patent classification devoted to lectins, which classification is comprised of at least 126 patents. Applicant contends that the issuance of 126 patents in the class 530, subclass 396 establishes the utility of the claimed invention because the skilled artisan would know how to use the invention for detecting and/or purifying molecules to which it binds and/or for its biological activities toward pathogens (first and second paragraphs on page 9 of the remarks).

These arguments have been fully considered but are not deemed persuasive. As repeatedly pointed out in previous Office Actions: the claimed polypeptide is shown in the specification to comprise limited sequence homology with a portion of three known collectin molecules; the alignments provide a comparison of the claimed polypeptide with short fragments of known collectins MBP and SP-A; the homology with MBP and SP-A proteins is extremely low even over these limited regions; and the homology with SP-D, the most closely related polypeptide, is only 35% (paragraph bridging pages 7-8). The Office Actions provide a detailed discussion of the relevant art (see especially the 29 April 2003 Office Action), which indicates that the degree of homology is too low to establish a specific and substantial utility for the claimed invention.

Applicant's arguments appear to be based on an assumption that all collectins have a patentable utility that is readily apparent to one of ordinary skill in the art and merely assigning the polypeptide to the collectin family suffices to meet Applicant's burden under 35 USC §101.

With regard to Applicant's citing the number of patents issued in a given class and subclass, this is not persuasive because, first, each patent application must be examined on its own merits and the allowance of similarly classified claims to others is immaterial to the allowability of the instant claims (see *In re Giolito*, 530 F.2d 397, 188 U.S.P.Q. 645 (C.C.P.A. 1976) and, second, a well-established utility must be specific to the subject matter claimed. Utilities such as, "detecting and/or purifying molecules to which [the claimed invention] bind[s] and/or for its biological activities toward pathogens", as suggested in Applicant's remarks, are neither specific nor substantial unless the application discloses, in specific terms, what molecules can be detected and purified using the claimed invention or how to use the biological activity towards pathogens, including which pathogens the invention is active against and how that activity can be applied to a real world use. These properties would not have been apparent to the skilled artisan based on the vague disclosure of the claimed invention in the specification.

Next, Applicant restates arguments previously made regarding the use of the claimed invention as a therapeutic having antibacterial and antiviral activity. In particular, Applicant cites MPEP §2107.03 and contends that evidence of close structural similarity to a compound known to have a particular therapeutic or pharmacological activity supports an assertion of therapeutic utility for a new compound (third paragraph on page 9).

This argument has been fully considered but is not deemed persuasive. MPEP §2107.03 instructs, "Office personnel should evaluate not only the existence of the structural relationship, but also the reasoning used by the applicant or a declarant to explain why that structural similarity is believed to be relevant to the applicant's assertion of utility."

As stated in the 28 October 2004 Office Action, page 8, there is nothing of record that would indicate that any collectin protein has an established therapeutic activity such that one of skill in the art would recognize all members of the collectin family as useful in therapeutic processes. In fact, van de Wetering *et al.*, cited by Applicant as Exhibit A and made of record in the 28 October Office Action, concludes, after a detailed review of the state of the art approximately five years after the effective filing date of the instant application, "[a] better understanding of collectin-mediated immunity may in the future allow the identification of disease states in which the therapeutic administration of collectins may be beneficial" (second full paragraph in the right column on page 1241). Furthermore, utilities such as "provid[ing] medical, experimental tools in which biological activities of the novel collectin are utilized", as asserted in the specification, are not specific and substantial utilities unless the biological activities of the novel protein are also disclosed in terms such that the skilled artisan would know specifically the "real world" use to which the medical, experimental tools can be applied (see the paragraph bridging pages 5-6 of the previous Office Action).

Even if therapeutic utility had been established for any one member of the collectin family, there is no evidence that all members of the collectin family would have the same therapeutic activity (*e.g.*, useful in the treatment of the same pathogen). Applicant acknowledges that collectins are a structurally diverse family of polypeptides. Consistent with the art cited in previous Office Actions, which teaches that the functional properties of proteins are related to their structure and proteins having distinct structure also exhibit distinct functional properties, members of the collectin family are known to be functionally diverse. For example, Lu *et al.* (2002) *Biochim. Biophys. Acta* 1572:387-400 teaches that each of the known collectins exhibit a

distinct profile of organisms recognized thereby (see especially Table 2). Therefore, even if the collectin SP-D was an established therapeutic for treatment for an organism such as *Mycobacterium tuberculosis*, which it is not, the skilled artisan would not know based on the disclosure that the claimed invention would also be useful in the treatment of *Mycobacterium tuberculosis*. Therefore, the specific useful properties of the claimed invention are not immediately apparent to the skilled artisan based on what has been disclosed in the application.

Thus, even if one accepts Applicant's assertion that the claimed invention is a member of the collectin family, assignment to this family does not support a well-established utility for what is presently claimed because there is no utility meeting the specific and substantial requirements of 35 U.S.C. §101 common to all members of the collectin family.

In the paragraph bridging pages 9-10 of the remarks, Applicant cites the Rule 1.132 declaration filed 9 August 2004 an urges that the showings therein confirm the claimed invention has utility as set forth in the specification.

The showings of the Declaration were addressed in the Office Action mailed 28 October 2004 (pages 10-11). As stated therein, the showings are insufficient to overcome the present rejection because they do not confirm a specific and substantial utility, which has basis in the specification. For reasons provided in previous Office Actions and herein above, the specification fails to disclose a specific and substantial asserted utility for the claimed invention and fails to disclose the properties of the invention such that a well-established utility would be readily apparent to the skilled artisan. Demonstrating that a fragment of the polypeptide comprised within the protein of the claims binds saccharides does not cure this deficiency because there is no asserted or well-established utility for a polypeptide that merely binds

saccharides. The declaration establishes that a portion of the polypeptide of the claims has one characteristic in common with collectins, as well as other lectins. It is noted, however, that the art recognizes many critical functional characteristics of collectins beyond merely binding to saccharides (see Holmskov (previously made of record) Chapter 5, pages 28-35).

In the first full paragraph on page 10 of the remarks, Applicant contends that the showing of the declaration that a fragment of the claimed invention exhibits selective binding of galactose "is an unexpected property" that is entirely dependent on the unique sequences of the claimed collectin polypeptide.

However, the post filing disclosure of an unexpected property that is not disclosed in the application and is not readily apparent from the disclosed characteristics of the claimed invention does not support a specific and substantial utility. On the contrary, the fact that the Declaration establishes specific binding properties of the claimed invention that would not have been predicted based on the structural characteristics disclosed in the application (*i.e.* are "unexpected") clearly shows that the application fails to teach the specific and substantial utility of what is claimed.

In the second full paragraph on page 10, Applicant again cites the teachings of Hoppe and Reid, which teachings were addressed in previous Office Actions. To summarize, Applicant particularly points out that Hoppe and Reid describe the common structure of collectins, which is consistent with the collectin claimed in the application and described in the specification. However, the Examiner can find no discussion of where the domains identified by Hoppe and Reid as characteristic of collectin proteins (See, *e.g.*, Fig. 1 and the caption thereto) can be found in the claimed polypeptide. Instead, it would seem that the claimed polypeptide has been

identified as a collectin based on similarity to a 27 amino acid fragment of MBP (Example 1). As pointed out by Applicant in the Paper filed 11 November 2003, "scavenger receptor proteins cannot take on an oligomeric form", which Hoppe and Reid show is characteristic of all collectins. Thus, the polypeptide of the present claims, being a scavenger receptor, would not be expected to form the higher order structure characteristic of collectins. Given this substantial departure from canonical collectin structure, and the low degree of overall similarity of the claimed invention to any protein belonging to the collectin family, one of ordinary skill would expect that there are specific functional characteristics of the invention, critical to its function and utility, which are not disclosed in the application. Therefore, the utility of the claimed invention would not be readily apparent to one of ordinary skill in the art at the time of filing.

Applicant next cites teachings from the post-filing art regarding the scavenger protein CL-P1, which is a membrane-bound collectin involved in the uptake of oxidized LDL particles. Applicant notes that the CL-P1 collectin shares 100% identity to the claimed polypeptide over 547 amino acids; that the polypeptide has been shown to recognize *E. coli* and *S. aureus*; and that the polypeptide preferentially binds galactose over mannose, which was demonstrated to be a property of the claimed polypeptide in the Rule 132 declaration filed 9 August 2004.

These Exhibits and arguments have been fully considered but are not deemed persuasive. It is first noted that art published after the effective filing date of the application is not probative of a well-established utility because the teachings therein were not available to the skilled artisan at the time the application was filed. In particular, at the time of filing, the skilled artisan was unaware of the binding of CL-P1 to LDL particles, *E. coli* and *S. aureus* or the binding of CL-P1 to galactose over mannose and, therefore, would not know that the CL-P1 protein would have

any utility related to binding LDL particles, *E. coli*, *S. aureus* or galactose. Furthermore, although the van de Wetering *et al.* reference cited as Exhibit A teaches that CL-P1 binds LDL particles, *E. coli* and *S. aureus*, there is no teaching in van de Wetering *et al.* to suggest that a patentable utility for a soluble fragment of CL-P1, which is what is presently claimed (see especially the paragraph bridging pages 6-7 of the 29 April 2003 Office Action), would be immediately apparent to one of ordinary skill in the art even in 2004 when van de Wetering *et al.* was published. Thus, the skilled artisan clearly would not have recognized that the fragment of CL-P1 presently claimed would be useful therapeutically as contemplated in the instant application.

In the first full paragraph on page 11, Applicant asserts that all that is required to meet the specific prong of utility under 35 USC §101 is that the claimed protein possess a utility that is not common to all proteins. This argument is not deemed persuasive. A "specific" is utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. The utilities asserted for the claimed invention are based on its general classification as a "lectin" which is a broad class of invention because it is comprised of proteins having divergent functional properties. As Applicant admits in the remarks, the specific carbohydrate binding properties of the claimed invention are "unexpected". This is clear evidence that the specific useful properties of the claimed invention are not disclosed and would not be apparent to the skilled artisan based on its classification as a "lectin".

In the third paragraph on page 11, Applicant contends that the Examiner's position is that every invention must have a "unique" utility. However, the Examiner has never suggested that the utility of the claimed invention must be unique. Instead, the Examiner's position is that the

utility must be specific to the subject matter claimed. The distinction is illustrated by the broad assertion that the claimed invention will bind a sugar based on its classification as a "lectin". A disclosure that a molecule is a "lectin" and therefore might bind a sugar does not constitute a specific utility because, as Applicant makes clear, the specific sugar bound by the claimed invention is an unpredictable (*i.e.*, "unexpected") property. In contrast, had the specification disclosed that the claimed invention binds galactose and therefore can be used to purify molecules comprising galactose, a specific utility would be apparent even though this utility might not be unique. However, in the instant case, there is no disclosure of the specific binding properties, or any other specific useful properties, of the claimed invention.

In the fifth full paragraph on page 11, Applicant construes the Examiner's statement that each collectin exhibits a distinct profile of organisms recognized thereby as inconsistent with the desirability of uniqueness. Applicant contends, "the proper way to interpret this evidence of 'distinct profile of organisms' is that *each collectin is useful* for its ability to recognize one or more organisms" (emphasis in the original).

This argument is not deemed persuasive because the issue with regard to 35 USC §101 is whether the application discloses a specific and substantial utility for what is claimed. Even if one accepts Applicant's contention that each collectin is useful for its ability to recognize one or more organisms, the skilled artisan does not know how to use the claimed invention if the organisms bound by the claimed collectin are not disclosed.

In the sentence bridging pages 11-12, applicant implies that one skilled in the art could perform carbohydrate binding studies or pathogen binding studies "to confirm well-established

utilities". Applicant further contends that evidence has been provided that confirms the claimed molecule has collection function.

These arguments are not deemed persuasive. First, the utility guidelines make clear that Applicant cannot saddle the skilled artisan with empirically confirming the asserted utilities. "Utilities that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use are not substantial utilities" (See the Revised Interim Utility Guidelines Training Materials at http://www.uspto.gov/web/menu/utility.pdf). Likewise, the Supreme Court in *Brenner v. Manson*, 148 USPQ 689, 695 (1966) concluded, "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field". Thus, it is Applicant's obligation under 35 USC §101 to disclose the claimed invention such that specific benefit exists in its currently available form.

With regard to "confirming" the function of the claimed molecule, Applicant admits in the instant remarks that the specific function of the tested fragment (*i.e.*, selective binding of galactose) is an unexpected property. Thus, contrary to confirming a specific utility that would be known to the skilled artisan based on the disclosed properties of the claimed invention, the post-filing evidence establishes that the specific useful properties of the claimed invention were unexpected. Therefore, it cannot be said that the post-filing evidence confirms a specific and substantial utility that was disclosed in the originally filed application.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §101 as lacking a patentable utility.

Claim Rejections - 35 USC § 112

Claims 157, 161-163, 166-168, 171-173, 176-178, 181-183, 186-188, 191-193, 196, 197, 199-202, 204-207, 209-212 and 214-219 **stand rejected** under 35 U.S.C. 112, first paragraph, as lacking an enabling disclosure.

As stated in the previous Office Action, since the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, even if a specific and substantial utility were identified, the skilled artisan would not be able to used the claimed invention as contemplated in the specification without undue experimentation.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The claims are directed to an isolated polypeptide having the amino acid sequence set forth as SEQ ID NO:2 (hereinafter referred to as the novel collectin) and fragments of said polypeptide. Additional claims are directed to polynucleotides encoding the novel collectin and nucleic acids that hybridize with the novel collectin under moderate stringency.

On page 47, the specification sets forth the industrial applicability of the claimed invention as, "useful for investigating mechanisms of biological defense systems, and may provide medical, experimental tools in which biological activities of the novel collectin are utilized. For example, vectors that can express the novel collectin, host cells comprising the vector with feasibility of expression, antibodies for the novel collectin, as well as probes for screening the related molecular species of the novel collectin can be provided. In addition, transgenic non-human animals...are provided, which may be utilized as disease model animals for studies on functions, or regulation of expression of the novel collectin".

Amount of direction provided by the inventor and existence of working examples: The specification discloses the sequence of the polypeptide comprising SEQ ID NO: 2, and the nucleic acid encoding said polypeptide, and generally teaches that the novel collectin might be involved in innate immunity based on homology to a family of proteins having Ca^{2+}-dependent carbohydrate recognition regions and collagen-like regions known as collectins. Figure 5 shows that an alignment of a 210 amino acid fragment of the instant protein with an 85 amino acid fragment of the 248 amino acid MBP, an 87 amino acid fragment of the 248 amino acid SP-A protein and a 207 amino acid fragment of the SP-D protein. The homology to the MBP and SP-A

proteins is extremely low, even over these limited regions, and, as pointed out in previous Office Actions, the homology with SP-D is only 35%.

With regard to using the invention to investigate mechanisms of biological defense systems or to provide medical, experimental tools, the teachings provided are generic in nature and provide no specific teaching as to what properties of biological defense systems can be elucidated, other than the properties of the claimed invention, or how the claimed invention can be used as a tool to solve any specific medical or experimental problem.

State of the prior art and level of predictability in the art: As described in previous Office Actions and herein above, the art available at the time the application was filed did not disclose a polypeptide having the properties of the claimed invention. As described in previous Office Actions, the art generally recognizes that functional properties of a polypeptide cannot be readily predicted based on the properties of polypeptides having similar structure. For example, Skolnick *et al.* (2000) *Trends Biotechnol.* 18:34-39 teach that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating specific details of protein function (see Box 2, page 36). Similarly, Bork (2000) *Genome Res.* 10:398-400 teaches that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially page 399). Smith *et al.* (1997) *Nature Biotechnol.* 15:1222-1223 teaches, "[t]ypical database searching methods are valuable for finding evolutionarily related proteins, but if there are only about 1000 major superfamilies in nature, then most homologs must have different molecular and cellular functions" (second column on page 132). These teaching demonstrate the unpredictability of assigning protein

function based on structure alone; and, given that the structural homology of the instant SEQ ID NO:2 to known collectins is 35%, at best, the function of the extracellular portion of the novel collectin described in the specification would be expected to be related to the function of other collectin family members in broad, general terms.

Furthermore, the art clearly recognizes that therapeutic application of any member of the generic collectin family was highly unpredictable at the time of filing. In particular, van de Wetering *et al.* (*supra*) concludes, after a detailed review of the state of the art approximately five years after the effective filing date of the instant application, "[a] better understanding of collectin-mediated immunity may in the future allow the identification of disease states in which the therapeutic administration of collectins may be beneficial" (second full paragraph in the right column on page 1241).

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to use the claimed invention as asserted in the specification without undue experimentation. Using the claimed invention contemplated in the specification requires that the functional properties of the polypeptide are known in sufficient detail such that the skilled artisan would know how results obtained using the claimed polypeptide or nucleic acid, or reagents developed therewith, elucidate the properties of the innate immune system or would know specifically what conditions could be treated and how those conditions could be treated using the claimed polypeptide or nucleic acid. However, there is no disclosure of the unique properties of the claimed polypeptide or nucleic beyond some limited homology with known members of the collectin family. Given the art recognized unpredictability of establishing protein function based

on similarity to proteins disclosed in databases and the absence of any established use of collectins as therapeutics, the skilled artisan clearly would not be able to use the invention as contemplated without having to engage in undue experimentation to establish the specific useful properties of the claimed polypeptide and nucleic acids.

For these reasons, the disclosure fails to adequately teach the skilled artisan how to use what is claimed. Therefore, the claims stand rejected under 35 USC §112, first paragraph.

Response to Arguments

In the remarks, Applicant contends that the experimental evidence made of record by the applicant largely renders the issue moot by confirming that the claimed polypeptide has collectin functions.

This argument has been fully considered but is not deemed persuasive. As discussed in previous Office Actions and herein above, the Application does not disclose the properties of the claimed invention such that the skilled artisan would know how to use what is claimed without having to determine the useful properties of the claimed invention by empirical experimentation. The only known functional property of the claimed invention (*i.e.*, a fragment of a CL-P1 receptor) is that it binds to galactose. However, there is no disclosure of galactose binding in the instant specification and Applicant admits that this property, to date the only function established for the claimed invention, is "unexpected". Therefore, the record as a whole shows that the skilled artisan would not have known how to use the claimed invention at the time the application was filed and determining how to use the claimed invention would require undue empirical experimentation, as the true function of the polypeptide would have been unexpected.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §112, first paragraph, as lacking an enabling disclosure.

Rejection of claims 162, 167, 169, 172, 177, 182, 187, 192 and 197 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment such that the claimed polynucleotide is limited to encoding a specifically disclosed amino acid sequence.

Claim 219 **stands rejected** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons of record. In the remarks at page 13, Applicant contends that the claim has been amended to explicitly recite polynucleotides or polypeptides set forth in the specification. However, claim 219 is directed to any polynucleotide that hybridizes, under any hybridization condition, with a probe comprising a disclosed sequence and that is an amplification product from a PCR reaction performed using specific primers, wherein the conditions of the PCR reaction are not specified. Clearly, the claimed polynucleotide is not limited to a polynucleotide set forth in the specification.

Rejection of claims 191, 206 and 216 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite is **withdrawn** in view of the amendments to the claims.

New Grounds Necessitated by Amendment

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 219 is rejected under 35 U.S.C. 102(b) as being anticipated by Entrez Nucleotide database entry F14786.

As discussed above, claim 219 is directed to any polynucleotide that hybridizes under any hybridization condition with a probe comprising a disclosed sequence and that is an amplification product from a PCR reaction performed using specific primers, wherein the conditions of the PCR reaction are not specified. Furthermore, the claim has been amended such that the claimed polynucleotide is no longer limited to encoding a polypeptide that binds to a carbohydrate in a Ca^{2+}-dependent manner. Given that any polynucleotide will hybridize to some extent with any other polynucleotide if the stringency of the hybridization conditions are sufficiently low and give that any polynucleotide can be non-specifically amplified in a PCR reaction given sufficiently low reaction conditions, the polynucleotide of claim 219 now reads on essentially all polynucleotides. Thus, the claim now reads on, e.g., the polynucleotide disclosed as entry F14786. Therefore, the claim is anticipated by the art.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M. Sullivan, Ph.D.
Examiner
Art Unit 1636

DANIEL M. SULLIVAN
PATENT EXAMINER